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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/575,660

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EXAMINER

BLAND, LAYLA D

ART UNIT

PAPER NUMBER

1623

MAIL DATE

DELIVERY MODE

07/03/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,660	Applicant(s) COTTICELLI ET AL.	
	Examiner LAYLA BLAND	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is a response to Applicant's amendment submitted April 28, 2008, wherein claims 1, 4-6, and 9-11 are amended and new claims 12-15 are added.

In view of Applicant's amendment submitted April 28, 2008, the rejection of claims 1, 4-6, 9, 10 and 11 under 35 USC 112, second paragraph, is withdrawn.

The following rejection is maintained and modified for relevancy to the currently amended claim set:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 9-11, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumbergs et al. (WO 92/00312, January 9, 1992, PTO-1449 submitted April 14, 2006).

Blumbergs et al. teach a process for the preparation of fludarabine phosphate. Fludarabine was dried to give essentially anhydrous material. Phosphorous oxychloride (523 mmol) was added to cold (0°C) trimethylphosphate (1L) and the solution was kept for 1 hour. Dried fludarabine was added with stirring to that solution. After stirring for a number of hours at 0°C, 8 L of methylene chloride was added to the solution. The

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methylene chloride was removed by decantation to leave a residual gummy mass.

Fludarabine phosphate was obtained from the gummy mass after purification. [page 3, line 20 – page 4, line 16] The appearance of a gummy mass in the methylene chloride solution is considered to be a precipitation. Trimethyl phosphate is preferred but tri-lower alkyl phosphate where the alkyl groups are 1 to 2 carbon atoms can also be used [page 3, lines 3-5].

Blumbers et al. also teach that, if the starting material nucleoside is not anhydrous, the yields are low due to a side reaction. Blumbers et al. do not state what the low yield was, but do note that 76% is markedly improved [page 3, lines 20-35].

Blumbers et al. do not teach the reaction at a temperature less than -5°C or -10°C , and suggest the use of anhydrous materials. Blumbers et al. also do not teach the claimed molar amounts of trialkyl phosphate or solvent.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out the reaction of Blumbers et al. at temperatures less than -5°C or -10°C , and to use air-dried starting materials. Blumbers teaches that the reaction does proceed using materials which are not anhydrous, although in lower yields due to side reactions. The skilled artisan would recognize that lowering the reaction temperature would decrease the likelihood of side reactions, and would also realize that lower temperatures would facilitate the precipitation of the product. Thus, the skilled artisan would have expected the reaction to proceed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the amounts of trialkyl phosphate used and solvent used

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by Blumbergs et al. The skilled artisan would have been motivated to reduce the amounts of solvent and trialkyl phosphate used because the reaction involves a precipitation, and the skilled artisan would realize that large amounts of solvent and/or excess reagent would impede precipitation. It is well-established that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Becket, 33 USPQ 33 (CCPA 1937). In re Russell, 439 F.2d 1228, 169 USPQ 426 (CCPA 1971).

Response to Arguments

Applicant argues that Blumbergs et al. do not teach or suggest using non-anhydrous fludarabine and that, using the claimed process, fludarabine phosphate can be obtained from fludarabine material that is not anhydrous. However, Blumbergs et al. do teach that the reaction does proceed using fludarabine that is not anhydrous, albeit in lower yields than the anhydrous process (76%). According to the specification, Applicants' process results in 40% yield, which is also substantially lower than Blumbergs' yield. Thus, Applicant's argument is not persuasive.

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumbergs et al. (WO 92/00312, January 9, 1992, PTO-1449 submitted April 14, 2006) in view of Wikipedia (Solvent).

Blumbergs et al. teach as set forth above.

Blumbergs et al. do not teach the use of hydrocarbon solvents or toluene.

Wikipedia teaches that dichloromethane and hydrocarbon solvents such as hexane, benzene, and toluene are all nonpolar solvents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize hydrocarbon solvents such as toluene instead of dichloromethane in the method taught by Blumberg et al. These are all nonpolar solvents and the skilled artisan would understand that they could be used interchangeably.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Tuesday - Friday, 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623

/Layla Bland/
Examiner, Art Unit 1623